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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/718,725	11/22/2000	William J. Boyle	A-378CIP2C3	5057

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/718,725	BOYLE ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61,63 and 65* is/are rejected.

7)☒ Claim(s) *62,64 and 66-75* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Prosecution is hereby reopened in view of the new grounds of rejection recited below. The indicated allowability of claims 61-75 is withdrawn in view of the new claim rejections set forth below. The Finality of the rejection of the last Office Action (02 April 2003) is *withdrawn*.

Status of Application, Amendments and/or Claims

The amendment filed 02 October 2003 has been entered. Claims 61-75 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The objection to claims 62, 64, 66-68, as set forth at page 3 of the previous Office Action (02 April 2003), is *withdrawn* in view of the amendment (02 October 2003).

The rejection to claims 61, 63, 65, 69-75 under 35 U.S.C. 112, first paragraph, scope of enablement, as set forth at pages 3-4 of the previous Office Action (02 April 2003), is *withdrawn* in view of the amendment (02 October 2003).

Claim Rejections-35 USC § 112, First Paragraph, Scope of Enablement

Claims 61, 63 and 65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

an antibody or fragment thereof which specifically **binds the amino acid sequence of SEQ ID NO:121 (or SEQ ID NO:123 or SEQ ID NO:125)**, wherein the sequence comprises an epitope recognized by the antibody

does not reasonably provide enablement for:

an antibody or fragment thereof which specifically **binds a portion of the amino acid sequence of sequence of SEQ ID NO:121 (or SEQ ID NO:123 or SEQ ID NO:125)**, wherein the portion comprises an epitope recognized by the antibody.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims encompass a vast genus of antibodies that need not bind to SEQ ID NOs:121, 123 and/or 125, yet the specification has not taught how to use these antibodies. An antibody or fragment thereof, which binds to an osteoprotegerin (OPG) protein will be made against the determinants/epitopes of the binding protein. There can be linear or conformational determinants. Epitopes formed by adjacent amino acid residues in the sequence are linear determinants. In contrast, conformational determinants are formed by amino acid residues from separated portions of the linear amino acid sequence that are spatially juxtaposed only upon folding. There are also neoantigenic determinants that result from modifications such as phosphorylation.

Protein folding, denaturation, and certain modifications will all affect the specificity of binding of an antibody to an epitope (see Abbas *et al.*, Cellular and Molecular Immunology, Second Edition. W.B. Saunders Company, Philadelphia , 1994).

It is well appreciated in the art of antibody production that it is unpredictable which amino acids are critical antigenic determinants (see Alexander *et al.,* Proc. Natl. Acad. Sci. 89:3352-3356, 1992). Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity (see Wells, Biochemistry 29:8509-8517, 1990 and Ngo *et al.,* The Protein Folding Problem and Tertiary Structure, pp. 433-440 and 492-495, 1994). Protein antigenicity can be significantly reduced by deletions of even a single residue. Further, even if an amino acid deletion does not destroy the activity of the immunizing protein, the change may significantly reduce the antigenicity of the protein (see Alexander *et al.*). The ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration; conformation is dependent upon surrounding residues. The specification does not provide sufficient guidance as to how to use antibodies that are specific to portions/fragments thereof of SEQ ID NOs:121, 123 and/or 125, which can be used for any specific purpose.

Due to the large quantity of experimentation necessary to generate the essentially limitless number of antibody variants recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding how to

use such antibodies, undue experimentation would be required of the skilled artisan to use the claimed invention in its full scope.

Due to the large quantity of experimentation necessary to generate the infinite number of antibody derivatives recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding how to use such antibodies, the absence of working examples directed to same, the complex nature of the invention, and the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Objections

Claims 62, 64, 66-75 are objected to for depending from a rejected claim.

Conclusion

Claims 61, 63 and 65 are rejected.

Claims 62, 64, 66-75 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RMD
6/29/06

MARIANNE P. ALLEN
PRIMARY EXAMINER
AU 1647

7/6/06